Agency for Healthcare Research and Quality
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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Red blood cell transfusion: a clinical practice guideline from the AABB.

Bibliographic Source(s)

Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, Holcomb JB, Illoh O, Kaplan LJ, Katz LM, Rao SV, Roback JD, Shander A, Tobian AA, Weinstein R, Swinton McLaughlin LG, Djulbegovic B, Clinical Transfusion Medicine Committee of the AABB. Red blood cell transfusion: a clinical practice guideline from the AABB. Ann Intern Med. 2012 Jul 3;157(1):49-58. [63 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Quality of evidence grades (high, moderate, low, very low) and strength of recommendations (strong, weak, uncertain) are defined at the end of the "Major Recommendations" field.

Question 1

In hospitalized, hemodynamically stable patients, at what hemoglobin concentration should a decision to transfuse red blood cells (RBCs) be considered?

Recommendations

- The AABB recommends adhering to a restrictive transfusion strategy.
- In adult and pediatric intensive care unit patients, transfusion should be considered at hemoglobin concentrations of 7 g/dL or less.
- In postoperative surgical patients, transfusion should be considered at a hemoglobin concentration of 8 g/dL or less or for symptoms (chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure).

Quality of evidence: high; strength of recommendation: strong

Question 2

In hospitalized, hemodynamically stable patients with preexisting cardiovascular disease, at what hemoglobin concentration should a decision to

transfuse RBCs be considered?

Recommendations

- The AABB suggests adhering to a restrictive transfusion strategy.
- Transfusion should be considered at a hemoglobin concentration of 8 g/dL or less or for symptoms (chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure).

Quality of evidence: moderate; strength of recommendation: weak

Question 3

In hospitalized, hemodynamically stable patients with the acute coronary syndrome, at what hemoglobin concentration should an RBC transfusion be considered?

Recommendation

The AABB cannot recommend for or against a liberal or restrictive RBC transfusion threshold. Further research is needed to determine the optimal threshold.

Quality of evidence: very low; strength of recommendation: uncertain

Question 4

In hospitalized, hemodynamically stable patients, should transfusion be guided by symptoms rather than hemoglobin concentration?

Recommendation

The AABB suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration.

Quality of evidence: low; strength of recommendation: weak

Definitions

Quality of Evidence

High - Indicates considerable confidence in the estimate of effect. The true effect probably lies close to the estimated effect, and future research is unlikely to change the estimate of the health intervention's effect.

Moderate - Indicates confidence that the estimate is close to the truth. Further research is likely to have an important effect on confidence in the estimate and may change the estimate of the health intervention's effect.

Low - Indicates that confidence in the effect is limited. The true effect may differ substantially from the estimate, and further research is likely to have an important effect on confidence in the estimate of the effect and is likely to change the estimate.

Very low - Indicates little confidence in the effect estimate. Any estimate of effect is very uncertain.

Strength of Recommendations

The strength of recommendations (for or against intervention) is graded as "strong" (indicating judgment that most well-informed people will make the same choice; "The AABB recommends. . ."), "weak" (indicating judgment that a majority of well-informed people will make the same choice, but a substantial minority will not; "The AABB suggests . . ."), or "uncertain" (indicating that the panel made no specific recommendation for or against interventions; "The AABB" cannot recommend . . .").

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Anemia and other conditions requiring red blood cell (RBC) transfusion

Guideline Category

Management

Risk Assessment

Clinical Specialty

Cardiology

Hematology

Internal Medicine

Orthopedic Surgery

Pediatrics

Surgery

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide clinical recommendations about hemoglobin concentration thresholds and other clinical variables that trigger red blood cell (RBC) transfusions in hemodynamically stable adults and children

Target Population

Hemodynamically stable adults and children who are candidates for red blood cell (RBC) transfusions

Interventions and Practices Considered

Use of transfusion thresholds ('triggers') as a means of guiding allogeneic and/or autologous red blood cell (RBC) transfusion

Major Outcomes Considered

- Proportion of patients who received transfusions with allogeneic or autologous red blood cells (RBCs) (primary outcome)

- Morbidity (nonfatal myocardial infarction, cardiac events, pulmonary edema, congestive heart failure, stroke, thromboembolism, renal failure, infection, hemorrhage, mental confusion)
- Death/mortality
- Hemoglobin levels (postoperative or postdischarge)
- Length of hospital stay
- Number of units transfused (LOS)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Search Methods for Identification of Studies

The search for trials was not restricted by date, language or publication status.

Electronic Searches

The Cochrane Injuries Group Trials Search Coordinator conducted the latest search for trials and collated the results. The following databases were searched:

- The Cochrane Injuries Group's Specialized Register (searched 1 February 2011)
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 1)
- MEDLINE (Ovid) 1950 to January Week 3 2011
- EMBASE (Ovid) 1980 to 2011 Week 04
- Institute for Scientific Information (ISI) Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to February 2011)
- ISI Web of Science: Conference Proceedings Citation Index - Science (CPCI-S) (1990 to February 2011)

The search strategies are presented in Appendix 1 in the systematic review (see the "Availability of Companion Documents" field).

Searching Other Resources

Experts in the field were contacted to identify information relevant to the review. Where possible, authors of published studies were contacted for clarification of trial methodology and data. This was only possible where a contact address was reported in the published study. The reference lists of relevant reviews and published papers as well as the reference lists of all included trials were searched for further studies.

Selection of Studies

Two authors independently screened the titles, abstracts, or both, of the search results and selected trials that met the previously defined inclusion criteria. The authors discussed inclusion of studies until consensus was reached; there were no disagreements on the inclusion of studies. The authors identified trials in which patients were randomized to a restrictive transfusion strategy (transfusion threshold and/or protocol), or to a control group which was randomized to a liberal transfusion strategy. The two authors independently extracted study characteristics and outcomes using a data extraction form. The extraction form recorded information regarding: study type, methodology descriptions, the presence of a transfusion threshold, transfusion protocol, the type of surgery involved, clinical setting, treatment outcomes and general comments.

Criteria for Considering Studies for the Review

Types of Studies

Randomized controlled trials with a concurrent control group. The reviewers included trials if the comparison groups were assigned on the basis of a clear transfusion 'trigger' or 'threshold, described as a hemoglobin or hematocrit level (with or without a specified level of hemodynamic instability) that had to be reached before a red cell transfusion was administered. Control group patients were required to be either transfused with allogeneic and/or autologous red blood cells (RBCs) at higher hemoglobin or hematocrit levels (transfusion threshold) than the intervention group or transfused in accordance with current transfusion practices, which may not have included a well-defined transfusion threshold, but involved liberal rather than restrictive transfusion practices.

Types of Participants

Trials of surgical or medical patients, involving adults and/or children, were included. Neonates were excluded.

Types of Interventions

The intervention considered was the use of transfusion thresholds ('triggers') as a means of guiding allogeneic and/or autologous RBC transfusion.

Types of Outcome Measures

Primary Outcomes

- The proportion of patients 'at risk' who were transfused with allogeneic and/or autologous RBCs.

Secondary Outcomes

- The amounts of allogeneic and autologous blood transfused
- Morbidity (non-fatal myocardial infarction, cardiac events, pulmonary oedema, cerebral vascular accident, thromboembolism, renal failure, infection, haemorrhage, mental confusion), mortality, haematocrit levels (postoperative/discharge) and length of hospital stay (LOS)

The reviewers expected the definitions of each of the morbidity events to vary between studies.

Number of Source Documents

The original literature search conducted in 1999 identified 110 full-text articles. Of these 110 eligible studies, 99 were excluded from further assessment (transfusion audits and reviews n = 94; observational studies - cohort or case-control studies n = 5). Eleven full-text articles were considered for review. Of these 11 studies one was excluded because the trigger was based on the level of sickle cell hemoglobin (HbS), not the hemoglobin or hematocrit level.

An updated search was conducted in November 2004. No new trials were identified by this search.

An updated search conducted in 2009 identified an additional seven trials. A further search conducted in February 2011 identified an additional two trials.

A total of 19 eligible studies were included in the systematic review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

High - Indicates considerable confidence in the estimate of effect. The true effect probably lies close to the estimated effect, and future research is unlikely to change the estimate of the health intervention's effect.

Moderate - Indicates confidence that the estimate is close to the truth. Further research is likely to have an important effect on confidence in the estimate and may change the estimate of the health intervention's effect.

Low - Indicates that confidence in the effect is limited. The true effect may differ substantially from the estimate, and further research is likely to

have an important effect on confidence in the estimate of the effect and is likely to change the estimate.

Very low - Indicates little confidence in the effect estimate. Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction and Management

Two authors performed data extraction on articles that met the inclusion criteria. One author then entered data into Review Manager; data were checked by the second author. The panel contacted authors of trials to request missing data.

A data extraction form was used to record data on the following outcomes: the number of patients exposed to allogeneic blood, the amount of allogeneic blood transfused, the number of patients receiving any transfusion (allogeneic blood, autologous blood, or both). For trials involving surgical patients, the following outcomes were recorded: postoperative complications (infection, hemorrhage, non-fatal myocardial infarction, cardiac events, renal failure, stroke, thromboembolism, pulmonary edema, mental confusion), mortality and length of hospital stay (LOS). Data for blood loss and hemoglobin and hematocrit levels (on admission, pre-post transfusion and at discharge) were recorded on the data extraction form as well as information regarding demographics (age, sex), type of surgery or medical condition. Data for allogeneic blood transfusion was extracted if it was expressed as packed red blood cells (RBCs). Information regarding the use of fresh frozen plasma (FFP) and/or platelets was documented.

Assessment of Risk of Bias in Included Studies

The Cochrane Collaboration's tool for assessing risk of bias is described in Section 8.5 of the *Cochrane Handbook for Systematic Reviews of Interventions*.

Two authors assessed the following domains for each study:

- Sequence generation
- Allocation concealment
- Blinding
- Incomplete outcome data
- Selective outcome reporting
- Other potential sources of bias

A "Risk of bias" table was completed for each study, incorporating a description of the study's performance against each of the above domains and the overall judgement of the risk of bias for each entry as follows: 'Low', 'Unclear' (indicating unclear or unknown risk of bias) and 'High' risk of bias.

Measures of Treatment Effect

The risk ratio for allogeneic blood transfusion in the intervention group as compared with the control group and the corresponding 95% confidence intervals (CIs) were calculated for each trial using the random-effects model (Der Simonian, 1986). A similar approach was adopted to examine the other outcomes of transfusion. The mean number of units of RBCs transfused to each group and the corresponding standard deviations were also entered. The mean difference (MD) and 95% CIs were used to express the average reduction in the number of units of RBC administered to the intervention group, compared with the control.

Unit of Analysis Issues

The unit of analysis was the patient. Data expressed in milliliters (ml) for the volume of blood transfused were converted to units of blood by dividing by 300.

Dealing with Missing Data

All analyses were on an intention-to-treat basis. No missing data were imputed.

Assessment of Heterogeneity

There was significant clinical heterogeneity. The trials included surgical, medical and critical care patients. The data for all outcomes were pooled and presented data stratified by subgroups for the primary outcome only. The subgroups evaluated were allogeneic transfusion, autologous transfusion and clinical settings (cardiac surgery, orthopedic surgery, vascular surgery, acute blood loss/trauma, cancer and critical care). Reviewers also examined the proportion of patients exposed to transfusion stratified by the transfusion threshold (difference ≥2 g/dL, <2 g/dL), risk of bias and units of blood transfused.

Statistical heterogeneity was examined using both the I^2 statistic and Chi^2 test. The I^2 statistic describes the percentage of total variation across studies due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity and larger values show increasing heterogeneity; substantial heterogeneity is considered to exist when the I^2 >50%. For the Chi^2 test, a P value of <0.10 was used to indicate the presence of statistically significant heterogeneity.

Assessment of Reporting Biases

Funnel plots were examined for evidence of publication bias. Although the small number of trials hampered funnel plot assessment, the outcome with the largest data set could be assessed for the presence of publication bias. The funnel plot for this outcome is presented in Figure 1 in the systematic review (see the "Availability of Companion Documents" field).

Data Synthesis

Due to the anticipated significant clinical heterogeneity of the trials, data were analyzed using a random-effects model.

All analyses were performed using Review Manager software. Data were entered into Review Manager on the numbers of patients exposed to allogeneic blood and the numbers of patients in each treatment group. Data in ml were converted to units by dividing by 300. Studies reporting hematocrit were converted to hemoglobin concentration by dividing by three.

Subgroup Analysis and Investigation of Heterogeneity

Subgroup analyses were performed to explore treatment effects by blood product (allogeneic versus autologous, units of blood transfused), clinical setting (cardiac surgery, orthopedic surgery, vascular surgery, cute blood loss/trauma, cancer, critical care), transfusion threshold (difference ≥2 grams per deciliter and difference less than 2 grams per deciliter) and risk of bias.

Sensitivity Analysis

A sensitivity analysis was performed to assess the effects of study allocation concealment on the results.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The AABB (formerly, the American Association of Blood Banks) commissioned and funded these guidelines through the AABB Clinical Transfusion Medicine Committee. In addition, the AABB Board of Directors directed the committee to recruit experts with interest in red blood cell (RBC) transfusion from other professional organizations.

Panel Composition

A committee of 20 experts was assembled. Twelve were current or former members of the AABB Clinical Transfusion Medicine Committee, whereas 6 were appointed by their respective professional organizations as subject matter experts. Fifteen of the physicians were pathologists or hematologists, most of whom had subspecialty expertise in transfusion medicine. The others included an anesthesiologist; a cardiologist; a pediatrician; experts in critical care medicine; trauma surgeons; specialists in internal medicine and systematic review; and a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist.

Grading of Evidence

The panel used the GRADE methodology to develop these guidelines. They prepared evidence profiles that display information on the effect of RBC transfusion in terms of benefits and harms for the most important clinical outcomes. The profiles also contained information on study limitations, consistency, directness, precision, and reporting bias. For each question or indication, the panel rated the importance of each outcome in influencing the decision to administer a transfusion to a patient. The outcomes were scored from 1 (not critical to making a decision) to 9 (critical to making a decision). The panel also rated the quality of evidence across all outcomes. The overall quality of the trials for each outcome was first assessed by 2 of the authors, after which a consensus of the entire panel was adopted. Each member of the panel was asked to make his or her final judgment on the strength of each recommendation and the overall quality of the body of evidence. The final quality rating and the strength of each recommendation were reached by consensus during an in-person meeting with the panel members.

Comments and Modification

The first author prepared the draft guideline document, which was modified and approved by all panel members and the AABB Clinical Transfusion Medicine Committee.

Rating Scheme for the Strength of the Recommendations

The strength of recommendations (for or against intervention) is graded as "strong" (indicating judgment that most well-informed people will make the same choice; "The AABB recommends. . ."), "weak" (indicating judgment that a majority of well-informed people will make the same choice, but a substantial minority will not; "The AABB suggests . . ."), or "uncertain" (indicating that the panel made no specific recommendation for or against interventions; "The AABB" cannot recommend . . .").

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

Internal Peer Review

Description of Method of Guideline Validation

The first author prepared the draft guideline document, which was modified and approved by all panel members and the AABB Clinical Transfusion Medicine Committee. Subsequently, the AABB Board of Directors reviewed and approved the guidelines.

Comparison with Other Guidelines

Recommendations from the British Committee for Standards in Haematology, the Australian and New Zealand Society of Blood Transfusion, and the European Society of Cardiology were discussed. See the "Comparison with Other Guidelines" section in the original guideline document for a comparison of recommendations.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

If a restrictive transfusion strategy were widely implemented and replaced a liberal strategy, exposure of patients to red blood cell (RBC) transfusions would decrease by an average of approximately 40% (relative risk, 0.61 [confidence interval (CI), 0.52 to 0.72]). This would have a large effect on blood use and the risks for infectious and noninfectious complications of transfusion.

Potential Harms

- Unnecessary transfusions increase costs and expose patients to potential infectious or noninfectious risks, such as hepatitis B and C virus, human immunodeficiency virus (HIV), transfusion-associated circulatory overload, transfusion-related acute lung injury, fatal hemolysis, life-threatening reaction, and fever.
- There was some uncertainty about the risk for perioperative myocardial infarction associated with a restrictive transfusion strategy. There was moderate heterogeneity between the results of the 2 major trials, and they were not large enough to precisely define the risks and benefits of transfusion in this setting.

Qualifying Statements

Qualifying Statements

- These guidelines focus on hemoglobin concentration thresholds and other clinical variables that might trigger red blood cell (RBC) transfusion. Practice guidelines are not intended as standards or absolute requirements and do not apply to all individual transfusion decisions. Clinical judgment is critical in the decision to transfuse; therefore, transfusing RBCs above or below the specified hemoglobin threshold may be dictated by the clinical context. Similarly, the decision not to transfuse RBCs to a patient with a hemoglobin concentration below the recommended thresholds is also a matter of clinical judgment.
- The strength of the recommendations included in these guidelines is limited by the paucity of clinical trial data in certain patient populations. The results of the 3 largest trials (TRICC, TRIPICU, and FOCUS) have not been replicated and do not include patients from many other populations who frequently receive transfusions. Clinical trials are needed in other patient populations that include (but are not limited to) patients with the acute coronary syndrome, elderly medical patients recovering from illnesses that result in hospitalization, patients with gastrointestinal bleeding, transfusion-dependent patients, patients with coagulopathy or hemorrhagic shock, and patients with traumatic brain injury. Furthermore, trials are needed to examine lower transfusion thresholds (for example, 6 g/dL), because the current evidence has examined thresholds of 7 g/dL in intensive care unit patients and 8 g/dL in other populations. This relative lack of clinical trial data is a barrier to wider acceptance of these guidelines.
- Guidelines cannot account for individual variation among patients. They are not intended to supplant physician judgment with respect to specific patients or special clinical situations. Accordingly, the AABB considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's unique circumstances.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, Holcomb JB, Illoh O, Kaplan LJ, Katz LM, Rao SV, Roback JD, Shander A, Tobian AA, Weinstein R, Swinton McLaughlin LG, Djulbegovic B, Clinical Transfusion Medicine Committee of the AABB. Red blood cell transfusion: a clinical practice guideline from the AABB. Ann Intern Med. 2012 Jul 3;157(1):49-58. [63 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Jul 3

Guideline Developer(s)

AABB - Nonprofit Organization

Source(s) of Funding

The AABB (formerly, the American Association of Blood Banks) commissioned and funded these guidelines through the AABB Clinical Transfusion Medicine Committee.

Guideline Committee

Clinical Transfusion Medicine Committee of the AABB

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Committee members had no substantial conflicts of interest as defined by the AABB conflict of interest policy. Pursuant to the policy, individual members were required to disclose actual and apparent financial, professional, or personal conflicts. Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M11-3065 .

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the Annals of Internal Medicine Web site .

Availability of Companion Documents

The following is available:

- Carson JL, Carless PA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev. 2012 Apr 18;4:CD002042. Electronic copies; Available from the PubMed Central® (PMC) Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 10, 2015. The information was verified by the guideline developer on September 22, 2015.

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